Remarks

Restriction Requirement

The claims were divided into three groups: group I, claims 1-9, drawn to a purified heparinase and method of its preparation; group II, claims 10-15, drawn to monoclonal antibodies cross-reacting with heparinase I and II; and group III, claims 16-17, drawn to an enzymatic method using heparinase to degrade heparin.

Applicants affirm their election of group I, claims 1-9. Claims 10-17 have been cancelled with the right to prosecute in divisional applications.

Response to Drawing Requirement

The objection to the drawings is noted and corrected formal drawings will be submitted when claims are allowed.

Rejections under 35 U.S.C. §112

The specification and claims have been objected to under §112 on the basis that the organism *F. heparinum* must be readily available to the public. This objection and rejection is respectfully traversed in view of the accompanying documents which indicates that the organism can be obtained from the American Type Culture Collection, Rockville, MD, without restriction.

Claim 4 has been rejected on the basis that only a specific stabilizing protein is enabled. This claim has been

cancelled although there are clearly many proteins other than albumin which could be used to stabilize the heparinase.

Claims 1 and 2 have been rejected as vague for the recitation "free of other lyase activity". The claims have been amended to recite "free of lyase activity other than heparinase II (or III) activity.

Claim 6 has been rejected on the basis that it is not clear if the cells are derived from a biologically pure culture; the claim has been amended to recite that it is a pure culture. The reference to the lysing step has not been further limited since methods for lysing bacteria are well known and one is not required to recite in a claim that which is well known, only that which constitutes the invention.

The mispelling of *Heparinum flavobacterium* in claims 1 and 2 has been corrected. The purified heparinases of claims 1-3 can be made by the method of claim 6-9. Claims 1 and 2 are directed to a purified protein so the reference to the source of the protein is not relevant with respect to the degree of purity; accordingly, these claims, unlike the method claims, have not been amended to recite that the culture is a biologically pure culture.

Rejection under 35 U.S.C. §103

Claims 1-9 have been rejected under 35 U.S.C. §103 as obvious over U.S. Patent No. 5,169,172 to Zimmerman, et al., in

combination with U.S. Patent No. 5,198,355 to Kikuchi, et al. These rejections are respectfully traversed.

Applicants agree with the substance of the Examiner's review of the art. However, neither Zimmerman nor Kikuchi recognized that there were two heparinases, **aside from heparinase I**, which were produced by *Flavobacterium heparinum*. As a result, although the techniques for isolating these proteins could be developed, following the guidelines of what is disclosed by the publications, there would have been no motivation to do so. Accordingly, the claimed purified heparinases cannot be obvious from the cited art.

Information Disclosure Statement

Pursuant to the duty of disclosure under 37 C.F.R. §1.56, applicants cite the following publications of which they are aware regarding heparinase. Copies of most of these publications are enclosed with the PTO form 1449 with this response; the remainder will be forwarded in a few days.

Patents

Horikoshi, Document No. 3108486 (Japan)

U.S. Patent No. 4,338,401 to Cremonesi

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These publications principally relate to the purification and cloning of heparinase I. None recognizes the existence of heparinase II and III, nor describes a method for how to isolate these two heparinases.

While this statement is believed to include all of the material art presently known to applicant, it should not be interpreted as a representation that an exhaustive search has been conducted or that no better art exists. Moreover, applicant invites the Examiner to make an independent evaluation of the cited art to determine its materiality and relevance to the subject matter of the present application. Applicant is of the opinion that his claims patentably distinguish over the art referred to herein, either alone or in combination.

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AMENDMENT AND INFORMATION DISCLOSURE STATEMENT

Allowance of claims 1-3, and 5-9, as amended, is respectfully requested.

Respectfully submitted,

Patrea L. Pabst
Reg. No. 31,284

Dated: November 8, 1993

KILPATRICK & CODY
1100 Peachtree Street
Suite 2800
Atlanta, Georgia 30309-4530
(404) 815-6508

CERTIFICATE OF MAILING (37 CFR 1.8a)

I hereby certify that this paper, along with any paper referred to as being attached or enclosed, is being deposited with the United States Postal Service on the date shown below with sufficient postage as first-class mail in an envelope addressed to the Commissioner of Patents and Trademarks, Washington, D.C. 20231.

Date: November 8, 1993

Patrea L. Pabst